

### **REMARKS**

Applicant submits these remarks in response to the Office Action dated October 2, 2003 ("Office Action"). Applicant hereby makes a Request for Continued Examination of the present application, pursuant to 35 U.S.C. § 132(b), as discussed with and agreed upon by the Examiner in a telephone communication on February 26, 2004. The three-month deadline for filing a response fell on January 2, 2004, therefore Applicant has filed a request for a two-month extension. Please charge any fee due in connection with this submission to Deposit Account No. 50-2212, Order Number 039751.0302546.

Claims 15-29 are pending in the application. The Examiner has objected to claims 15-21 and 24 for being dependent on canceled claim 14. Claims 15-21 have been amended to depend from claim 29.

The Examiner has objected to claims 17-24 for repeating the phrase "wherein said." Claims 17, 20, 21, 24, 27 and 28 have been amended to correct the typographical error noted in the Examiner's objection. This amendment does not alter the scope of those claims. The Applicant believes that claims 15-21 and 17-24 are now in condition for allowance.

Claim 22 has also been amended to more clearly recite, "extending either said first primer or said second primer towards the other." This recitation was already present in claim 29 and does not constitute an introduction of new matter. Claims 22 and 29 have both been amended to add the recitation, "wherein said target sequences are immobilized on a solid phase surface." This amendment to claims 22 and 29 is not an introduction of new matter. Support for this amendment is found in the application at p. 69, ll. 22-26 and in the last paragraph of p. 79. At p. 69, l. 22, the application teaches that "the target nucleic acid is immobilized on a solid-phase surface" in the oligonucleotide ligation assay. The ligation assay, in which the target nucleic acid can be immobilized on a solid-phase surface, is described in combination with extension in the last paragraph of p. 79, "Combination of ligation and extension," which describes ligation probes that "do not hybridize adjacently; rather, they are separated by one or more bases." Thus, the application disclosure supports the requirement of a target nucleic acid immobilized on a solid-phase surface in the methods of claims 22 and 29.

**Claim Rejections—35 U.S.C. § 112**

The Examiner has rejected claims 22-28 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Office Action at p. 3, ¶ 4.

The Examiner wrote that claims 22-28 are indefinite in Claim 22, step a) for the recitation “the first primer” because the recitation lacks proper antecedent basis in the claim.

Claim 22 has been amended to more clearly point out the claimed invention. The amendment to make clear that the recitation of “first primer” is the first recitation of the “first primer” in claim 22 does not alter the scope of the claim. Claims 23, 24, 26, 27 and 28 depend from claim 22, which contained the recitation cited by the Examiner as lacking proper antecedent basis. Applicant believes that the amendment made to claim 22 to recite “a first primer” has overcome the Examiner’s rejections to claims 22-28 and that claims 22-28 are now in condition for allowance.

**Claim Rejections—35 U.S.C. § 103(a)**

**Macevicz (US 6,280,935) in view of Ullman *et al.* (US 5,185,243)**

The Examiner has rejected claims 29, 15-17, 19-20, 22-24 and 26-27 under 35 U.S.C. § 103(a) as being unpatentable over Macevicz in view of Ullman *et al.* Office Action at pp. 3-6.

**Macevicz (US 6,280,935) in view of Ullman *et al.* (US 5,185,243) and further in view of Walt *et al.* (US 6,327,410)**

The Examiner has also rejected claims 18 and 25 under 35 U.S.C. § 103(a) as being unpatentable over Macevicz in view of Ullman *et al.* as applied to claims 22 and 29 and further in view of Walt *et al.* Office Action at pp. 7-8. Applicants respectfully traverse this rejection.

**Barany (US 6,027,889) in view of Ullman *et al.* (US 5,185,243) and Walt *et al.* (US 6,327,410)**

In addition, the Examiner rejected claims 15-29 under 35 U.S.C. § 103(a) as being unpatentable over Barany *et al.* in view of Ullman *et al.* and Walt *et al.* Office Action at pp. 8-14.

Applicants respectfully assert that these rejections are no longer applicable to claims 15-29, as amended to more clearly state the claimed invention.

None of the references alone, or in combination, suggest or make obvious:

“A method for simultaneously detecting at least sixteen target nucleic acid sequences comprising:

- a) hybridizing a first primer of at least sixteen pairs of primers to a first portion of at least sixteen target sequences, wherein each primer pair is specific for a different sequence, wherein said target sequences are immobilized on a solid phase surface, and wherein said first primer further comprises an adapter sequence;
- b) hybridizing a second primer of said primer pairs to a second portion of said target sequences;
- c) extending either said first primer or said second primer towards the other;
- d) ligating said first and second primers together to form a modified primer;
- e) contacting said adapter sequence of said modified primer or its complement with an array comprising:
  - i) a substrate with a surface comprising discrete sites; and
  - ii) a population of microspheres comprising at least a first subpopulation comprising a first capture probe, such that said first capture probe and an amplification product of said modified primer form a hybridization complex; wherein said microspheres are distributed on said surface; and
- f) detecting the presence of said modified primer.”

In addition, none of the references, alone or in combination, suggest or make obvious a method of detecting target nucleic acid sequences comprising:

- “a) hybridizing a first primer to a first portion of a target sequence, wherein said target sequences are immobilized on a solid phase surface,
- b) hybridizing a second primer to a second portion of said target sequence wherein said first portion of said target sequence and said second portion of said target sequence are not adjacent;
  - c) extending either said first primer or said second primer towards the other;
  - d) ligating said first and second primers together to form a modified primer;
  - e) contacting said adapter sequence of said modified primer or its complement with an array comprising:
    - i) a substrate with a surface comprising discrete sites; and

- ii) a population of microspheres comprising at least a first subpopulation comprising a first nucleic acid capture probe, such that said first capture probe and an amplification product of said modified primer form a hybridization complex; wherein said microspheres are distributed on said surface; and
- f) detecting the presence of said modified primer to thereby detect said nucleic acid sequence.”

Therefore, none of claims 15-29 would be rendered obvious by any of the references cited by the Examiner, alone, or in combination.

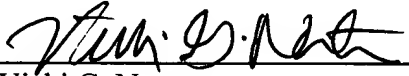
#### Conclusion

Applicants believe that the Amendments made to claims 15-22, 24, and 27-29 have put them in condition for allowance. Applicants further believe that for the reasons set forth above, the rejections of claims 15–29 have been overcome or are no longer applicable. Withdrawal of the rejections are respectfully requested.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (858) 847-4321.

Respectfully submitted,

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